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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/544,180	MOHNEN ET AL.	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *6-10,14,15 and 17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-13,16 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/4/05; 5/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on July 9, 2007 from Donna M. Ferber, the election with traverse of group I, claims 1-5, 11-13, 16, and new claim 25, is acknowledged.

The Applicant traverses on the grounds that Groups I and II should be rejoined because they are all nucleic acids encoding members of the GALAT enzyme family (see third paragraph on page 8 of the response received on July 9, 2007). This is not persuasive, because nucleic acids encoding members of the GALAT enzyme family were known in the prior art (see Shinn et al), and therefore, the claims lack unity of invention *a posteriori.*

The Applicant further traverses on the grounds that polypeptides and the nucleic acids encoding them have unity of invention *a priori* (see fourth paragraph on page 8 of the response). This is not persuasive, however, because a search of the prior art found nucleic acids encoding GALAT enzymes (see Shinn et al), and therefore the claims lack unity of invention *a posteriori.*

The Applicant elects SEQ ID NO:2 for examination, and states that it is an election of a particular species for examination (see paragraph bridging pages 8-9 of the response). This is not correct, because this is not a species election. Each individual GALAT enzyme is a separate invention. Each polypeptide identified by a

sequence identifier was in a separate group for the restriction, because they are separate inventions. This is not an election of species. This is an election of a single invention to be examined.

Claims 1-25 are pending in the instant application.

Claims 6-10, 14, 15, and 17-24 are withdrawn from consideration because they are directed to non-elected inventions.

Claims 1-5, 11-13, 16, and 25, as they relate to SEQ ID NO:2, are examined in this Office Action.

The Applicant is advised to amend the claims to read only on the elected amino acid sequence, SEQ ID NO:2, and the nucleic acid encoding it, SEQ ID NO:1.

The restriction requirement is MADE FINAL.

Specification

2. The specification is objected to because the Brief Descriptions of the Drawings does not include a description for each of the parts A, B, C, and D for Figure 3. The Applicant is advised to amend the description to describe each section of Figure 3, individually.

3. The specification is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. On page 15, line 12 and lines 29-30;

page 16, lines 23-24; page 17, line 16; page 23, line 13; page 25, line 26; and page 26, line 26, there are embedded links. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP 608.01.

4. The use of the trademark SEPHAROSE has been noted in this application. It should be written in all capital letters wherever it appears; or alternatively, it should be denoted with the registered trademark symbol, ®, and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The abstract is objected to because it should specify the gene that has been elected for prosecution.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: - - NUCLEIC ACIDS ENCODING A GALACTURONOSYLTRANSFERASE (GALAT1) ENZYME FROM ARABIDOPSIS - - .

Information Disclosure Statement

7. The listing of references in the specification on pages 65-75 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

8. Claims 3, 5, 11, and 12 are objected to for the following reasons:

Claim 3 is objected to because of the following informalities: it is technically incorrect. The recitation of "wherein the amino acid molecule is selected from the group consisting of the sequences..." lacks agreement between the amino acid molecule and the sequences. The Applicant is advised to replace "molecule" with - - sequence - - . Appropriate correction is required.

Claim 11 is technically incorrect. Claim 1 has been amended such that the nucleic acid of claim 1 already comprises a promoter, therefore, the vector of claim 11 now comprises two promoters. The Applicant is advised to amend claim 11 to replace "in operable linkage the nucleic acid according to claim 1 and a plant

expressible promoter" with - - the nucleic acid of claim 1 wherein the regulatory sequence is a promoter that functions in plants - - .

Claims 5 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

For claim 5, the polypeptide in claim 4 can be encoded by the nucleic acid sequence of SEQ ID NO:1; therefore the statement that it is encoded by SEQ ID NO:1 does not further limit the polypeptide; and, given the current claim construction, claim 5 depends only on the polypeptide. In order to further limit claim 5, the Applicant is advised to amend claim 5 to recite - - wherein the nucleic acid comprises SEQ ID NO:1 - - . This suggested amendment would further limit the nucleic acid.

For claim 12, the limitation that the promoter is heterologous to the nucleic acid is already included because the independent base claim, claim 1, includes the recitation that "said sequences are not associated together in nature" which is interpreted to mean that they are heterologous sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 3-5 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

Claim 3 recites the limitation "the amino acid molecule" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In addition, claim 3 continues to recite a whole list of sequences, when only SEQ ID NO:2 was elected for prosecution. The Examiner is unable to determine if claim 3 is supposed to encompass only a nucleic acid that encodes SEQ ID NO:2, or if the claim is supposed to continue to encompass fragments and 50% identity. For the purpose of examination, the claim is interpreted broadly to encompass fragments of SEQ ID NO:2 and polypeptides with approximately 50% identity to SEQ ID NO:2. Claims 4 and 5 are also constructed in a way that does not clearly limit the nucleic acid. It is unclear if the nucleic acid must encode the full-length protein of SEQ ID NO:2, because the claim construction does not limit the nucleic acid, it only limits the polypeptide, and the wording seems to continue to encompass nucleic acids encoding fragments and polypeptides with 50% similarity to SEQ ID NO:2. For the purpose

of examination, the claims are interpreted broadly to encompass fragments of SEQ ID NO:2 and polypeptides with approximately 50% similarity to SEQ ID NO:2.

Claim 25 recites the limitation "the coding sequences" in line 1. Claim 3 does not include a reference to "coding sequences". There is insufficient antecedent basis for this limitation in the claim. Furthermore, the only sequence that has been elected for prosecution is SEQ ID NO:1 which encodes SEQ ID NO:2; therefore, claim 25 should be amended to recite only the elected sequence of SEQ ID NO:1.

10. Claims 1-5, 11-13, 16, and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to isolated nucleic acids encoding a polypeptide or a fragment thereof having galacturonosyltransferase (GalAT) activity, and to polypeptides or fragments having 50% similarity with SEQ ID NO:2, and to vectors and plants comprising said nucleic acids. It is noted that claim 3 is interpreted to encompass fragments of SEQ ID NO:2 and polypeptides having approximately 50% identity to SEQ ID NO:2 (see 112, 2nd paragraph, rejection, above). It is also noted that claims 4 and 5 depend from claim 3, and therefore, they have the same issues

of indefiniteness. They will also be interpreted broadly to encompass fragments of SEQ ID NO:2 and polypeptides having approximately 50% identity to SEQ ID NO:2.

The essential feature of the nucleic acids of the instant invention is that they encode polypeptides that have GalAT activity (see page 7, lines 6-7).

The Applicants describe the nucleic acid of SEQ ID NO:1 (also referred to as At3g61130) which encodes the polypeptide of SEQ ID NO:2 (see pages 28-29 and the sequence listing). The Applicants describe a bioinformatics search that identified 10 genes with 23-29% sequence identity, and they describe several motifs and conserved residues that are present in these genes (see page 18 and figure 7). The Applicants describe this polypeptide as having GalAT activity (see page 9, lines 24-25 and Figure 8).

The Applicants do not describe any fragments of SEQ ID NO:2 that are sufficient for GalAT activity. Nor do they describe any polypeptides having 50% identity to SEQ ID NO:2 that are known to have GalAT activity.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See

University of California v. Eli Lilly and Co., 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of fragments of SEQ ID NO:2 that have GalAT activity or polypeptides having as little as 50% identity to SEQ ID NO:2 that have GalAT activity, and they fail to describe a representative number of nucleic acids encoding such fragments and polypeptides. The Applicants only describe the polypeptide of SEQ ID NO:2, and one nucleic acid encoding it, SEQ ID NO:1. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of polypetides that have GalAT activity. They merely disclose motifs found in a bioinformatics search utilizing amino acid sequences for which there has not been any activity empirically determined. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for GalAT activity, it remains unclear what features identify polypeptides capable of such activity. Since the genus of polypetides and nucleic acids encoding such polypeptides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

SEQ ID NO:2 consists of 673 amino acids. Polypeptides that are fragments of SEQ ID NO:2 can be as small as di-peptides, therefore, this genus of molecules encompasses over 200,000 molecules. Polypeptides that have as little as 50%

identity to SEQ ID NO:2 can have 336 amino acid substitutions within the polypeptide; therefore, this genus of molecules encompasses 20^{336} molecules. Nucleic acids encoding these polypeptides encompass an even larger genus of molecules because of codon redundancy.

Nucleic acids that encode fragments of SEQ ID NO:2 and polypeptides with as little as 50% identity to SEQ ID NO:2 encompass multitudes of molecules, many of which would not produce a polypeptide with GalAT activity upon being transcribed in a plant cell, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have only reduced one molecule to practice in an experiment that demonstrates GalAT activity. Accordingly, the specification fails to provide an adequate written description to support the genus of nucleic acids that encode fragments of SEQ ID NO:2 or polypeptides with 50% identity to SEQ ID NO:2 that comprise GalAT activity as set forth in the claims. (See Written Description guidelines published in the Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices: p. 1099-1111).

11. Claims 1-5, 11-13, 16, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding the full-length polypeptide of SEQ ID NO:2, and vectors and plants comprising such nucleic acids, does not reasonably provide enablement for nucleic acids encoding fragments of SEQ ID NO:2 or encoding polypeptides with approximately 50% similarity to SEQ ID NO:2. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to isolated nucleic acids encoding a polypeptide or a fragment thereof having galacturonosyltransferase (GalAT) activity, and to polypeptides or fragments having 50% similarity with SEQ ID NO:2, and to vectors and plants comprising said nucleic acids. It is noted that claim 3 is interpreted to encompass fragments of SEQ ID NO:2 and polypeptides having approximately 50% identity to SEQ ID NO:2 (see 112, 2nd paragraph, rejection, above). It is also noted that claims 4 and 5 depend from claim 3, and therefore, they have the same issues of indefiniteness. They will also be interpreted broadly to encompass fragments of SEQ ID NO:2 and polypeptides having approximately 50% identity to SEQ ID NO:2.

The Applicants teach the nucleic acid of SEQ ID NO:1 (also referred to as At3g61130) which encodes the polypeptide of SEQ ID NO:2 (see pages 28-29 and the sequence listing). The Applicants disclose a bioinformatics search that identified 10 genes with 23-29% sequence identity, and they teach several motifs and conserved residues that are present in these genes (see page 18 and figure 7). However, none of the other genes identified have been shown to encode proteins that have GalAT activity. The Applicants teach that the polypeptide of SEQ ID NO:2 (At3g61130) has GalAT activity (see page 9, lines 24-25 and Figure 8).

The Applicants do not teach any fragments of SEQ ID NO:2 that are sufficient for GalAT activity. Nor do they teach any polypeptides having 50% identity to SEQ ID NO:2 that are known to have GalAT activity.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain GalAT activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making substitutions in proteins does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with

alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1).

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding multitudes polypeptides with 50% identity to SEQ ID NO:2, or polypeptides that are fragments of SEQ ID NO:2. Making all possible single amino acid substitutions in a 673 amino acid long protein such as SEQ ID NO:2 would require making and analyzing 19^{673} nucleic acids; these proteins would have 99.9% identity to SEQ ID NO:2. Because nucleic acids encoding proteins with 50% identity to SEQ ID NO:2 would encode proteins with 336 amino acid substitutions, many more than 19^{673} nucleic acids would need to be made and analyzed.

The state of the prior art is such that one of skill in the art cannot predict how many amino acid substitutions can be tolerated and which residues can be substituted without losing enzymatic activity. For example, Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to

mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with 336 amino acid substitutions that also have GalAT activity would require undue experimentation.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of skill in the art to make and use the multitudes of polypeptides encompassed by the claims.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to make and use the claimed invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Khan A. A. (US Patent No. 5,294,593, issued on Mar. 15, 1994).

Claim 16 is drawn to progeny of a plant that is transformed with a nucleic acid encoding a GalAT enzyme.

Khan teaches a seed, which is a progeny of a parent plant (see columns 4-11 and all claims). Because the plant recited in instant claim 13 can be heterozygous for the nucleic acid molecule, seeds produced by the plant may not comprise the nucleic acid molecule. 50% of seeds produced from crossing a heterozygous transgenic plant with a wild-type plant do not comprise the transgene, and 25% of seeds produced from self-pollination of a heterozygous transgenic plant do not comprise the transgene. Therefore, the seeds taught by Khan are indistinguishable from non-transgenic seeds (progeny) encompassed by the instant claim 16. The Applicant is advised to amend the claim to include the recitation - - wherein said progeny comprises said expression vector - - .

13. No claim is allowed.

Allowable Subject Matter

14. Nucleic acids that comprise a polynucleotide that encodes a protein comprising SEQ ID NO:2 are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cathy K. Worley
Patent Examiner
Art Unit 1638

CKW